

Use of cold dry air provocation with acoustic rhinometry in detecting nonspecific nasal hyperreactivity

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ABSTRACT

Background: Cold dry air provocation is useful for evaluating nonspecific nasal hyperreactivity. However, there is no research on nasal volume and dimensions after cold dry air provocation. In this respect, acoustic rhinometry is a useful tool in objectively assessing nasal cavity volume and dimension. The goal of this study was to evaluate nonspecific hyperreactivity using cold dry air provocation with acoustic rhinometry.

Methods: Cold dry air provocation with acoustic rhinometry was performed on 21 healthy volunteers (group A), 24 patients with allergic rhinitis (group B), and 32 patients with nonallergic rhinitis (group C). The change in symptoms using a visual analog scale (VAS), amount of rhinorrhea, and change of total nasal volume (TNV) and minimal cross-sectional area (MCA) were measured in all three groups.

Results: The two patient groups showed greater change in nasal symptoms (VAS, 2.0 ± 2.3 in group C versus 0.9 ± 1.8 in group A), more rhinorrhea (0.4 ± 0.7 g in group B and 0.3 ± 0.3 g in group C versus 0.1 ± 0.1 g in group A), and greater change in total nasal volume (TNV) and MCA. The patient group with history of nonspecific hyperreactivity showed more rhinorrhea (0.5 ± 0.7 g versus 0.1 ± 0.2 g) and greater change in TNV and MCA (TNV, $56.8 \pm 39.5\%$ versus $18.0 \pm 17.0\%$; MCA, $86.6 \pm 81.0\%$ versus $11.5 \pm 9.7\%$).

Conclusion: Cold dry air provocation with acoustic rhinometry could be a useful adjunct tool for detecting nonspecific hyperreactivity.

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Key words: Acoustic rhinometry, cold dry air, dimension, minimal cross-sectional area, nasal cavity, nasal volume, nonallergic, nonspecific hyperreactivity, provocation, rhinorrhea

Patients with allergic or nonallergic rhinitis often experience nasal congestion, rhinorrhea, or sneezing triggered by several non-specific physical stimuli such as sudden temperature change, smoking, or chemical pollutants.¹ Researchers have developed a number of nasal provocation protocols for the evaluation of nonspecific hyperreactivity. Among these, cold dry air provocation is superior to histamine challenge in determining nonspecific hyperreactivity of nasal cavity in nonallergic patients.² For this reason, “nonspecific hyperreactivity” was defined as “increased responsiveness to cold dry air” for the clear definition of terms in this study.

Cold dry air could activate inflammatory pathways such as mast cell degranulation and increase vascular permeability. The pathophysiology of this reaction is probably related to the drying effect on the nasal mucosa caused by prolonged cold dry air inhalation.³ In fact, one could easily imagine that cold dry air stimulation results in decreased volume and dimensions of nasal cavity. Although Shusterman *et al.* used rhinomanometry to evaluate the change of nasal airway resistance after cold dry air provocation,⁴ there are no studies of nasal volume and dimensions after such provocation. For this, acoustic rhinometry is a useful tool in objectively assessing nasal cavity volume and dimension.⁵ The aim of this study was to detect nonspecific hyperreactivity by evaluating the change in symptoms, amount of rhinorrhea, and changes in volume and dimension of nasal cavity using cold dry air provocation with acoustic rhinometry.

MATERIALS AND METHODS

Subjects

Twenty-one healthy volunteers (group A, 13 men and 8 women, 20–65 years old), 24 patients with allergic rhinitis (group B, 12 men and 12 women, 22–53 years old), and 32 patients with nonallergic rhinitis (group C, 15 men and 17 women, 16–65 years old) were enrolled based on inclusion and exclusion criteria (Table 1). There were no significant differences in age or sex distribution of patients among the three groups. The study was approved by the Inha University Institutional Review Board Committee on Studies Involving Human Beings.

Cold Dry Air Challenge

Patients were acclimatized to room temperature (20°C) for 15 minutes before blowing their nose to remove nasal secretion and nasal rinsing five times with normal saline irrigation. Approximately 15 minutes after humidification, baseline symptom scores for nasal obstruction, rhinorrhea, sneezing, and itching were obtained using a visual analog scale (VAS). The VAS uses a 10-cm line with a dot at every centimeter, and patients mark the severity of their symptoms from 0 to 10 on the line. Total nasal volume (TNV) and minimal cross-sectional area (MCA) were obtained by acoustic rhinometry in both nasal cavities. The method for performing acoustic rhinometry is well described elsewhere.⁵

Cold dry air provocation test was then performed on each patient. Air for medical uses was cooled to $\sim 0^\circ\text{C}$ by passing through a refrigerant air dryer. The cooled air was dried ($<10\%$ humidity), by passing through a mist separator and a micromist separator, and passed through the filter to remove particles, dust, and any microorganisms. The cold dry air was delivered to patients' noses via a pediatric CPAP (continuous positive airway pressure) mask. Patients were instructed to inhale through the nose and exhale through the mouth during the air challenge and to maintain their ordinary breathing frequency. Approximately 400 L of cold dry air was supplied over 6 minutes. For patient safety, the provocation was stopped immediately in the case of hyperventilation or other major discomfort.

Five minutes after provocation, the change in symptom scores was measured using VAS. A precision scale (Mettler, Würzburg, Germany) was used to measure the amount of rhinorrhea after provoca-

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Table 1 Study inclusion and exclusion criteria

Inclusion criteria for the whole cohort
Aged 16–65 yr old
Inclusion criteria for healthy volunteers (Group A)
Free of any nasal symptoms
Negative skin-prick test or MAST results to any antigens
Inclusion criteria for allergic rhinitis patients (Group B)
More than 1 yr of suffering from allergic rhinitis
Typical symptoms of allergic rhinitis such as watery rhinorrhea and sneezing
Strong positive (>3+) response to house-dust mites
Inclusion criteria for nonallergic rhinitis patients (Group C)
More than 1 yr of suffering from nonallergic rhinitis
Negative skin-prick test or MAST results to any antigens
Exclusion criteria
Use of inhaled or systemic corticosteroid within a month
Use of inhaled cromoglycates, astemizole, or nedocromil sodium within a month
Inability to stop medication that could affect nasal function
A serious or unstable, systemic disease
Pregnant or lactating woman
History of nasal surgery within 3 mo
Presence of nasal polyp or chronic sinusitis (evaluated by plain x ray or CT of paranasal sinus)
Exposure to chemical irritants
Smoking

MAST = multiple allergosorbent test.

tion with an accuracy of 0.01 g. The examiner measured the weight of several sheets of tissue paper before and after patients blew their nose using that tissue paper. TNV and MCA were obtained in both nasal cavities by repeating acoustic rhinometry, and the changes were expressed as a percentage. The larger of the values between the right and left nasal cavity was selected. To avoid diurnal variation and inter-test error, all the provocations were performed at a regular time during the day by a single experienced examiner.

Statistical Analysis

Because the data were not normally distributed, the Mann-Whitney test was used to compare the change in symptoms; amount of rhinorrhea, TNV, and MCA among the three groups; and to evaluate differences within each group (with or without nonspecific hyperreactivity). Data were reported as mean $\pm$ SD. SPSS 12.0 Statistics Software (SPSS, Inc., Chicago, IL) was used and $p < 0.05$ was accepted as statistically significant.

RESULTS

On the VAS scale, group C showed significantly greater change in nasal obstruction (2.0 ± 2.3 versus 0.9 ± 1.8 ; $p < 0.05$) and rhinorrhea ($p < 0.05$) than group A. Changes in sneezing and itching were not significantly different (Fig. 1). There were no significant differences between groups A and B on all VAS measures.

Patients in groups B and C had more rhinorrhea (group B, 0.4 ± 0.7 g, and group C, 0.3 ± 0.3 g, versus group A, 0.1 ± 0.1 g; $p < 0.01$) and significantly greater change in TNV and MCA ($p < 0.01$) than those in group A (Fig. 2). The changes in TNV and MCA correlated with each other in both direction and extent of change at the individual level.

Patients in groups B and C ($n = 56$) were divided into nonhyperreactive ($n = 23$) and hyperreactive individuals ($n = 33$) based on subjective complaints of nonspecific hyperreactivity to cold dry air such as cold air in winter or air conditioner. Hyperreactive individuals had significantly more rhinorrhea (0.5 ± 0.7 g versus 0.1 ± 0.2 g;

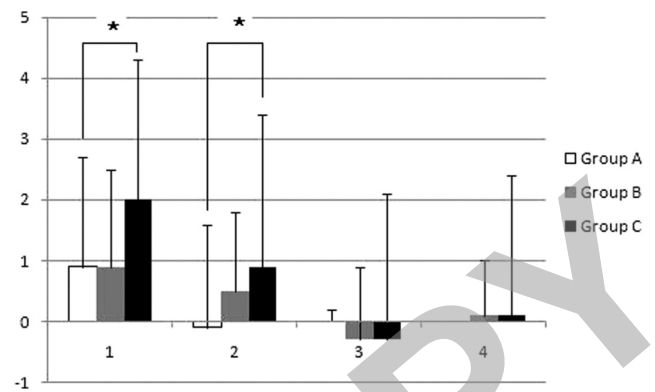


Figure 1. Symptom change after cold dry air provocation. Group A, healthy volunteers; group B, allergic rhinitis; group C, nonallergic rhinitis. Categories: 1, nasal obstruction; 2, rhinorrhea; 3, sneezing; and 4, itching (* $p < 0.05$). Error bar represents SD.

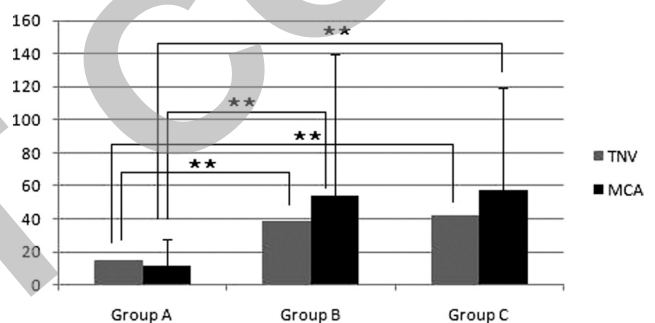


Figure 2. Change in total nasal volume (TNV) and minimal cross-sectional area (MCA; %) after cold dry air provocation (** $p < 0.01$). Error bar represents SD.

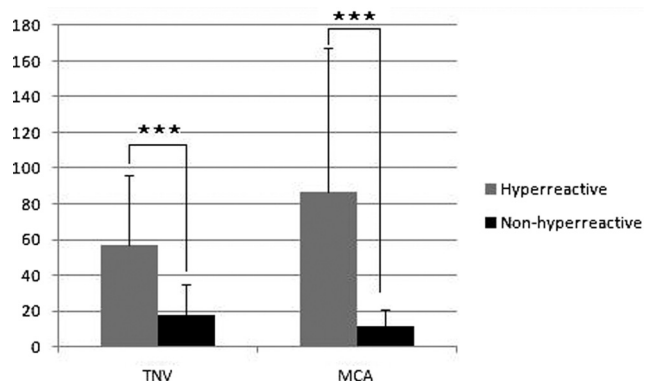


Figure 3. Comparison of change in total nasal volume (TNV) and minimal cross-sectional area (MCA) between patients with and without nonspecific hyperreactivity (** $p < 0.001$). Error bar represents SD.

$p < 0.001$) and greater change in TNV ($56.8 \pm 39.5\%$ versus $18.0 \pm 17.0\%$) and MCA ($86.6 \pm 81.0\%$ versus $11.5 \pm 9.7\%$; $p < 0.001$) compared with nonhyperreactive counterparts (Fig. 3). Of note, none of the healthy volunteers reported hyperreactivity. Comparing the individual MCA data of hyperreactive patients with those without hyperreactivity, it was evident that each individual with hyperreactivity had a greater change in MCA than those without hyperreactivity (Fig. 4).

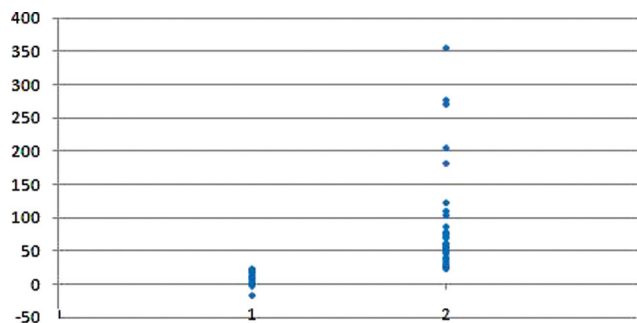


Figure 4. Display of minimal cross-sectional area data in each patient with or without hyperreactivity as individual points (1, without hyperreactivity; 2, with hyperreactivity).

DISCUSSION

Nasal hyperreactivity is an increased sensitivity of the nasal response to a normal stimulus. In this study, nonspecific hyperreactivity was defined as increased responsiveness to cold dry air. Its pathogenesis is unclear but includes damage to the epithelial barrier, increased sensitivity of irritant receptors in the nasal mucosa, changes in neuronal transmission, change in release or degradation of mediators, changes in metabolism or receptor sensitivity of target cells, and influx of inflammatory cells.⁶

Several methods, such as methacholine challenge, histamine challenge, capsaicin challenge, and cold dry air challenge, are available for the laboratory study of nasal hyperreactivity. Cold dry air is known to induce symptoms of nasal obstruction, rhinorrhea, and occasional sneezing in susceptible individuals with a history of subjective discomfort on exposure to cold dry air such as winter weather or air conditioners. Responses to cold dry air seem to be independent of any known underlying condition of the nasal cavity.³ There are several studies using cold dry air to assess autonomic nervous responses,⁶ response after topical steroid treatment,⁷ inflammatory mediators,⁸ comparison with histamine challenge,² and osmolality of nasal secretion.³ However, there is no research on the amount of rhinorrhea or the volume and cross-sectional area of the nasal cavity itself.

In this study, patients with allergic or nonallergic rhinitis showed significantly greater change in nasal symptoms compared with healthy volunteers, but there were no differences in sneezing or itching. This is consistent with the results from other studies. According to Cruz *et al.*, pruritus and sneezing rarely occur after cold dry air provocation.⁷ Togias *et al.* reported that hyperosmolality produces nasal symptoms.⁹ They observed an ipsilateral and contralateral secretory response after local application of hypertonic saline to the nasal mucosa. In this study, the absolute amount of rhinorrhea was higher in the patient group than in healthy volunteers. A possible explanation for this is an increase in osmolality caused by increased inflammatory mediators, proteins, and exudates rather than a pure increase in water in the nasal secretion.

The principle of acoustic rhinometry is based on sound reflection. By acoustic rhinometry, clinicians can determine the total volume of the nasal cavity and the MCA using a rapid, painless, and noninvasive technique. Nasal provocation test with acoustic rhinometry uses house-dust mite antigens to provoke the nasal cavity, and the resulting change in TNV and MCA is calculated as a percentage. Kim *et al.* reported that the severity of skin-prick test results correlates well with the degree of change in TNV and MCA.⁵ Moreover, new standards for clinical use have been developed, making acoustic rhinometry a very useful tool for improving the practice of evidence-based medicine in rhinology.¹⁰

Both allergic and nonallergic patients showed greater change in TNV and MCA than did the healthy volunteers. To evaluate hyperreactivity, patients in the allergic and nonallergic groups were di-

vided into those with and those without nasal hyperreactivity based on patient history. Using this classification, individuals susceptible to cold dry air showed a greater degree of TNV and MCA change and more rhinorrhea, which correlates with other studies. Throughout this study, there were no differences in symptom change, amount of rhinorrhea, and change in TNV or MCA between allergic and nonallergic subjects. This result is consistent with a report by Togias *et al.* that nonallergic physical stimuli could not differentiate between allergic and nonallergic patients, although both groups showed higher reactivity than healthy volunteers.³

The main strength of this study is the relatively large number of enrolled patients compared with other studies. Despite a relatively large sample size, SDs in the data were large and this could be improved by enrolling more patients. Because the results were not normally distributed, parametric analyses such as ANOVA were not possible, as was encountered in other studies.^{2,8}

In the experimental design, the provocation machinery delivered cold air at $\sim 0^{\circ}\text{C}$, which is higher than other studies. Because of this, patients complained less of discomfort despite increased rhinorrhea and decreased volume of nasal cavity and were more cooperative with the provocation test. Because the authors adopted a single provocation protocol, which requires a relatively short time to perform, this test could be useful in the outpatient setting.

Our study is important in establishing the usefulness of cold dry air provocation with acoustic rhinometry for detecting and evaluating nonspecific hyperreactivity. Additional studies with more patients are needed to define the diagnostic standards for this technique by developing a receiver-operator curve to determine cutoffs for specificity and sensitivity of the test.

CONCLUSIONS

Nonspecific hyperreactivity of the nasal cavity was objectively assessed based on the change in symptoms, amount of rhinorrhea, and change in acoustic rhinometry parameters using a cold dry air provocation test and acoustic rhinometry. Therefore, cold dry air provocation with acoustic rhinometry could be a useful adjunct tool in detecting nonspecific hyperreactivity.

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